Complete Summary

GUIDELINE TITLE

Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jun. 45 p. (Technology appraisal guidance; no. 121).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

High-grade (grade 3 and 4) glioma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Internal Medicine
Neurological Surgery

Neurology
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of carmustine implants and temozolomide in the treatment of newly diagnosed high-grade glioma

TARGET POPULATION

Patients with newly diagnosed high-grade glioma

INTERVENTIONS AND PRACTICES CONSIDERED

1. Carmustine implants as an adjunct to surgery and radiation
2. Temozolomide

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Overall and progression-free survival
    - Quality of life
    - Adverse events
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG), Peninsula Medical School and Wessex Institute for

Health Research and Development, University of Southampton (see the "Availability of Companion Documents" field.)

Clinical Effectiveness

Inclusion and Exclusion Criteria

Inclusion

Carmustine-impregnated Wafers (BCNU-W)

Intervention:

BCNU-W as an adjunct to surgery with subsequent radiation therapy with or without standard systemic chemotherapy.

Comparators:

- Placebo wafer inserted at the time of surgery with or without radiotherapy (RT).
- Surgery with or without RT and systemic chemotherapy with standard antineoplastic agents (excluding those listed in the intervention).

Temozolomide (TMZ)

Intervention:

Surgery followed by RT with concomitant TMZ followed by an adjuvant course of temozolomide.

Comparators:

Surgery followed by RT with or without systemic chemotherapy with standard antineoplastic agents (excluding those listed in the intervention).

Inclusion Criteria Common to Both Interventions

Population:

Children and adults with newly diagnosed Grade III or IV primary gliomas.

Study design:

- Systematic reviews
- Randomised controlled trials (RCTs)
- Non randomised evidence was also considered where it gave the best estimates of a required parameter (for example adverse effects or patient preferences) or where RCT data was scanty or uninformative.

Exclusion

BCNU-W

Studies of BCNU-W in which treatment with carmustine other than as wafers at the time of surgery and radiation therapy took place but was not reported separately.

TMZ

Studies in which the use of TMZ other than as an adjunct to surgery and radiation therapy took place but was not reported separately.

Exclusion Criteria Common to Both Interventions

Population:

- Not primary diagnosis of high-grade glioma (low-grade gliomas, other types of brain tumor)
- Not newly diagnosed glioma (recurrent or advanced cases)

Study design:

- Narrative or non-systematic reviews
- Preclinical or biological studies, animal models
- Case studies
- Abstract only
- Not available in English

Search Strategy

Electronic databases were searched for published systematic reviews, RCTs, observational studies, economic evaluations and ongoing research in March 2005 and updated in August 2005. Appendix 4 of the Assessment Report (see the "Availability of Companion Documents" field) shows the databases searched and the strategy in full. Bibliographies of articles were also searched for further relevant studies, and the U.S. Food and Drug Administration (FDA) website was searched for relevant material.

Observational studies were considered for inclusion to broaden the evidence-base under review, as it was suspected that there would be few relevant RCTs. Moreover, it was judged that the more inclusive eligibility criteria frequently found in observational case series might result in evidence with a greater degree of generalizability than the RCTs. Additionally, the Assessment Group speculated that such studies might provide longer follow-up data and more detailed description of treatment-related adverse effects.

Identification of Studies

Identification of relevant studies was made in two stages. Abstracts returned by the search strategy were examined independently by two researchers and screened for inclusion or exclusion. Disagreements were resolved by discussion. Full texts of the identified studies were obtained. Two researchers examined these

independently for inclusion or exclusion and disagreements were resolved by discussion.

The process is shown in Appendix 5 of the Assessment Report (see the "Availability of Companion Documents" field).

Cost-Effectiveness

Search Strategy and Critical Appraisal Methods

Electronic databases were searched using the strategy shown in Appendix 4 of the Assessment Report (see the "Availability of Companion Documents" field).

Inclusion and Exclusion Criteria

Studies were included if they were complete economic evaluations:

- Of TMZ as adjuvant and concomitant chemotherapy to surgery and RT
- Of BCNU-W as adjuvant chemotherapy to surgery and RT
- In newly diagnosed high grade gliomas
- Cost-utility studies
- Relevant to the United Kingdom setting

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

The Assessment Group identified two randomised controlled trials (RCTs) that compared the effectiveness of carmustine implants plus radiotherapy with that of placebo plus radiotherapy, and two RCTs of temozolomide plus radiotherapy compared with radiotherapy alone. No studies comparing carmustine implants with temozolomide, or comparing carmustine implants or temozolomide with other antineoplastic agents (for example, the PCT chemotherapy regimen [procarbazine, lomustine, and vincristine], were identified.

Cost-Effectiveness

There are as yet no published economic evaluations of treatment comparisons involving BCNU-W.

Two published analyses assess the resource consumption related to treating high grade glioma in the UK National health service (NHS) context.

Two economic analyses were submitted to National Institute for Health and Clinical Excellence (NICE) by the industry sponsors of Gliadel® (BCNU-W) and Temodal® (TMZ):

- A report of a modelling-based cost-utility analysis of debulking surgery with BCNU-W versus debulking surgery with placebo wafers.
- A report of a trial-based cost-effectiveness analysis of RT with concomitant and adjuvant TMZ versus RT only

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG) Peninsula Medical School and Wessex Institute for Health Research and Development, University of Southampton (see the "Availability of Companion Documents" field.)

Data Extraction Strategy

Data were extracted by one researcher and checked by another. Actual numbers were extracted where possible. Data extraction forms for each included study are reproduced in Appendix 7 of the Assessment Report (see the "Availability of Companion Documents" field).

Quality Assessment Strategy

Assessments of randomised controlled trial (RCT) quality were performed using the indicators shown below. Results were tabulated and these aspects described.

Internal Validity

Sample Size

- Power calculation at design

Selection Bias

- Explicit eligibility criteria
- Proper randomisation and allocation concealment
- Similarity of groups at baseline

Performance Bias

- Similarity of treatment other than the intervention across groups

Attrition bias and Intention to Treat Analysis

- Are all patients accounted for?
- Are withdrawals specified and described?
- Was analysis undertaken on an intention to treat (ITT) basis?

Detection Bias

- Blinding
- Objective outcome measures
- Appropriate data analysis

The Assessment Group also noted any potential conflicts of interest (for example, financial support provided to studies and/or authors by manufacturers of the interventions).

For observational studies, the Assessment Group addressed such of these criteria as were applicable to study design, and also noted whether the study in question was prospective and whether it explicitly enrolled consecutive patients.

Systematic reviews were assessed against Quality of Reporting of Meta-Analyses (QUOROM) guidelines.

External Validity

External validity was judged according to the ability of a reader to consider the applicability of findings to a patient group in practice. Study findings can only be effectively generalisable if they (a) describe a cohort that is representative of the affected population at large or (b) present sufficient detail in their outcome data to allow the reader to extrapolate findings to a patient group with different characteristics.

To assess the generalisability of included studies, the Assessment Group focused on the baseline factors on which high-grade glioma outcomes are known to be substantially dependent -- age, performance status and tumor histology. Studies that were representative with regard to these factors were judged to have high external validity. The age-range of each cohort, in particular, was seen as an index of a study's applicability to the patient population in practice.

Methods of Analysis

Details of the methodology and results of included studies are tabulated and described in the text (refer to the Assessment Report [see the "Availability of Companion Documents" field]). The Assessment Group has presented results from RCTs and case series in the same tables; where study design renders cells inapplicable, they have been grayed out. Dashes in the tables indicate the

information was not reported. X^2 statistics were derived using the CHIDIST function of Microsoft Excel.

Where data were available the Assessment Group combined absolute survival at a fixed time point (e.g., at 12 months). Meta-analysis was undertaken to estimate a weighted treatment effect across trials. A random effects model was used to avoid the assumption of a single underlying treatment effect. This is more conservative, but incorporates an estimate of between-study heterogeneity. Without patient level data, it was not possible to pool survival analyses.

Indirect comparison between the two interventions was considered if enough similarities in study method and population were found.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document

and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The manufacturer of carmustine implants submitted an economic model that estimated the cost per quality-adjusted life year (QALY) of carmustine implants plus radiotherapy, compared with placebo plus radiotherapy. The manufacturer of temozolomide submitted a within-trial economic analysis of radiotherapy plus temozolomide compared with radiotherapy alone. The Assessment Group reviewed both manufacturers' analyses. The Assessment Group also constructed their own economic model, which was designed to estimate the cost effectiveness of carmustine implants and the cost effectiveness of temozolomide.

See section 4.2 in the original guideline document for a detailed discussion of cost effectiveness models from the manufacturers and the Assessment Group.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups

- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Temozolomide and carmustine implants have been appraised separately for the treatment of newly diagnosed high-grade glioma. On the basis of the evidence presented to the Committee, no recommendation can be made regarding the sequential use of these treatments for newly diagnosed high-grade glioma.

- Temozolomide, within its licensed indications, is recommended as an option for the treatment of newly diagnosed glioblastoma multiforme (GBM) in patients with a World Health Organization (WHO) performance status of 0 or 1 (see Appendix C of the original guideline document for WHO performance status classification).
- Carmustine implants, within their licensed indications, are recommended as an option for the treatment of newly diagnosed high-grade glioma only for patients in whom 90% or more of the tumour has been resected.
- Treatment with carmustine implants should be provided only within specialist centres that in general conform to guidance in 'Improving outcomes for people with brain and other central nervous system tumours' (National Institute for Health and Clinical Excellence [NICE] cancer service guidance 2006; www.nice.org.uk/csgbraincns), and should be supervised by specialist neurosurgeons who spend at least 50% of their clinical programmed activities in neuro-oncological surgery. The specialists should also have access to:
    - Multidisciplinary teams to enable preoperative identification of patients in whom maximal resection is likely to be achievable
    - Magnetic resonance imaging (MRI) to enable preoperative identification of patients in whom maximal resection is likely to be possible, and
    - Image-directed technology, such as neuronavigation, for use intraoperatively to assist the achievement of maximal resection
- Carmustine implants are not recommended for the treatment of newly diagnosed high-grade glioma for patients in whom less than 90% of the tumour has been resected.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of carmustine implants and temozolomide in patients with newly diagnosed high-grade glioma

POTENTIAL HARMS

Carmustine

Adverse effects include brain edema, convulsions, healing abnormalities, and intracranial infections.

Temozolomide

Adverse effects include anorexia, constipation, fatigue, headache, lymphopenia, nausea, neutropenia, thrombocytopenia, and vomiting.

For full details of side effects and contraindications, see the summary of product characteristics (SPC) available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "'Healthcare standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by

Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

- NICE has developed tools to help organisations implement this guidance (listed below). These are available on NICE website (www.nice.org.uk/TA121) (see also "Availability of Companion Documents" field).
    - Local costing template incorporating a costing report to estimate the savings and costs associated with implementation
    - Audit criteria to monitor local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jun. 45 p. (Technology appraisal guidance; no. 121).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Jun

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Professor A E Ades, MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol; Dr Amanda Adler, Consultant Physician, Addenbrooke's Hospital, Cambridge; Dr Tom Aslan, General Practitioner, Stockwell, London; Professor David Barnett (*Chair*) Professor of Clinical Pharmacology, University of Leicester; Mrs Elizabeth Brain, Lay member; Professor Karl Claxton, Professor of Health Economics, University of York; Dr Richard Cookson, Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital; Professor Christopher Eccleston, Director, Pain Management Unit, University of Bath; Dr Paul Ewings, Statistician, Taunton and Somerset NHS Trust; Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford; Mr John Goulston, Director of Finance, Barts and the London NHS Trust; Mr Adrian Griffin, Health Outcomes Manager, Johnson & Johnson Medical Ltd; Ms Linda Hands, Consultant Surgeon, John Radcliffe Hospital, Oxford; Dr Elizabeth Haxby, Lead Clinician in Clinical Risk Management, Royal Brompton Hospital; Dr Rowan Hillson, Consultant Physician, Diabeticare, The Hillingdon Hospital; Dr Catherine Jackson, Clinical Senior Lecturer in Primary Care Medicine, University of Dundee; Professor Philip Home (*Vice Chair*) Professor of Diabetes Medicine, Newcastle University; Dr Terry John, General Practitioner, The Firs, London; Professor Richard Lilford, Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmingham; Dr Simon Maxwell, Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Queen's Medical Research Institute, University of Edinburgh; Dr Simon Mitchell, Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester; Ms Judith Paget, Chief Executive, Caerphilly Local Health Board, Wales; Dr Ann Richardson, Lay member; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Mr Mike Spencer, General Manager, Clinical Support Services, Cardiff and Vale NHS Trust; Dr Debbie Stephenson, Head of HTA Strategy, Eli Lilly and Company; Professor Andrew Stevens, Professor of Public Health, University of Birmingham; Dr Cathryn Thomas, General Practitioner and Associate Professor, Department of Primary Care and General Practice, University of Birmingham; Dr Simon Thomas, Consultant Physician, General Medicine and Clinical Pharmacology, Newcastle Hospitals NHS Trust; Mr David Thomson, Lay member; Dr Norman Vetter, Reader,

Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff; Professor Mary Watkins, Professor of Nursing, University of Plymouth; Dr Paul Watson, Medical Director, Essex Strategic Health Authority

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jun. 2 p. (Technology appraisal 121). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Costing template and report: carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jun. Various p. (Technology appraisal 121). Available in Portable Document Format (PDF) from the NICE Web site.
- Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. Audit criteria. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jun. 14 p. (Technology appraisal 121). Available in Portable Document Format (PDF) from the NICE Web site.
- The effectiveness and cost-effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma: a systematic review and economic evaluation. NHS R&D HTA programme. Peninsula Technology Assessment Group, Exeter, UK. 2005 Sep 27. 243 p. Electronic copies: Available from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1267. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 Jun. 4 p. (Technology appraisal 121).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1268. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on August 1, 2007.

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their Technology Appraisal guidance with the intention of disseminating and facilitating the implementation of that guidance. NICE has not verified this content to confirm that it accurately reflects the original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE technology appraisal guidance is prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/29/2008